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O. Zuccaro, M.E. Tosti, A. Mele,
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Epidemiology of acute viral hepatitis in Italy: results of the surveillance through SEIEVA (Sistema Epidemiologico Integrato dell'Epatite Virale Acuta)

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Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute

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2012, v, 24 p. Rapporti ISTISAN 12/4

This report describes epidemiological changes in acute viral hepatitis in Italy in the past two decades. The hepatitis A virus circulation progressively decreased. The incidence of symptomatic hepatitis A is 1.1/100,000/year in interepidemic periods. Shellfish consumption and travelling to areas endemic are still the most important risk factors. The impact of hepatitis B virus, hepatitis Delta virus, and hepatitis C virus, in Italy is on decline. Currently, the incidence of symptomatic acute hepatitis B, C and Delta is 0.9/100,000/year, 0.2/100,000/year and 0.2/1,000,000/year, respectively. For hepatitis B and C the most important risk factors are cosmetic treatments, dental therapy, promiscuous sexual activity and, only for hepatitis C, also intravenous drug use and surgery. Until recently, acute infection with the hepatitis E virus was considered to be confined to persons who had travelled to endemic areas. However, it is now considered to be an emerging disease, with an increasing number of indigenous cases.

Key words: Italy, Epidemiology, Viral hepatitis, Hepatitis A, Hepatitis B, Hepatitis Delta, Hepatitis C, Hepatitis E, Surveillance, Risk factors, Incidence, Prevalence

Istituto Superiore di Sanità
Epidemiologia delle epatiti virali acute in Italia: risultati della sorveglianza attraverso il SEIEVA (Sistema Epidemiologico Integrato dell'Epatite Virale Acuta).
Ornella Zuccaro, Maria Elena Tosti, Alfonso Mele, Enea Spada e il Gruppo di collaborazione SEIEVA
2012, v, 24 p. Rapporti ISTISAN 12/4 (in inglese)

Questo rapporto descrive i cambiamenti dell'epidemiologia delle epatiti virali acute avvenuti in Italia nelle ultime due decadi. La circolazione del virus dell'epatite A in Italia è progressivamente diminuita. Nei periodi interepidemici l'incidenza di epatite A sintomatica è 1,1/100.000/anno. Il consumo di frutti di mare e i viaggi in aree ad alta endemia sono ancora i principali fattori di rischio. L'impatto del virus B, del virus Delta e del virus C dell'epatite in Italia è in riduzione. Attualmente l'incidenza di epatite acuta sintomatica B, C e Delta è rispettivamente 0,9/100.000/anno, 0,2/100.000/anno e 0,2/1.000.000/anno. Per l'epatite B e C i principali fattori di rischio sono i trattamenti estetici, la terapia odontoiatrica, l'attività sessuale promiscua e, solo per l'epatite C, l'uso di droghe per via endovenosa e gli interventi chirurgici. L'epatite E, prima considerata un'infezione principalmente confinata ai viaggiatori in aree endemiche, oggi si configura come malattia emergente, con un crescente aumento del numero di casi autoctoni.

Parole chiave: Italia, Epidemiologia, Epatite virale, Epatite A, Epatite B, Epatite Delta, Epatite C, Epatite E, Sorveglianza, Fattori di rischio, Incidenza, Prevalenza

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ACUTE VIRAL HEPATITIS: THE ITALIAN SURVEILLANCE SYSTEM

Background, aims and method

SEIEVA (Sistema Epidemiologico Integrato dell'Epatite Virale Acuta: Integrated Epidemiological System of Acute Viral Hepatitis) is the Italian national surveillance system for Acute Viral Hepatitis (AVH). It was created in 1985 and is coordinated by the National Centre for Epidemiology, Surveillance and Health Promotion of the Istituto Superiore di Sanità (the National Institute of Health in Italy).

The overall objective of SEIEVA is to promote the local and national surveillance and control of AVH (1). The specific objectives are:

- to estimate the incidence of the specific types of AVH, by date of onset, geographic area, age and sex;
- to estimate the proportion of infected individuals exposed to specific risk factors, by type of AVH;
- to evaluate the specific role played by the considered risk factors for each type of AVH;
- to define and develop appropriate control strategies;
- to perform early detection of AVH outbreaks, followed by case-control or cohort studies and molecular epidemiologic analyses to identify the source and modes of transmission and implement appropriate and timely outbreak-control measures.

The data collected by SEIEVA are provided by Local Health Units (Aziende Sanitarie Locali, ASLs), which participate on a voluntary basis.

For each suspected case of AVH, the treating hospital, healthcare facility, or physician sends the mandatory notification to the ASL; an ASL physician then interviews the individual using a standardized questionnaire developed for SEIEVA.

This questionnaire includes socio-demographic, clinical and laboratory information, and information on risk factors (faecal-oral risk factors in the six weeks prior to disease onset and parenteral risk factors in the previous six months).

Following the interview, serological tests are performed, the results of which are later recorded on the questionnaire, in particular: HBsAg, IgM anti-HBc, IgM anti-HAV (Hepatitis A Virus), anti-HCV (Hepatitis C Virus), HCV-RNA, anti-Delta and IgM anti-HEV (Hepatitis E Virus). Data on IgM anti-HEV have been collected since 2008, which is one of the innovative activities of SEIEVA.

The ASLs send the completed questionnaires to the Coordination Centre at the Istituto Superiore di Sanità, where data are entered in a centralised database and analysed. Since 2007, it has been possible for the ASLs to enter data directly using a specifically developed website. This process allows to investigate more quickly and accurately outbreaks.

In the event of an outbreak, an epidemiological investigation is carried out to identify possible sources and modes of transmission of the virus; when possible, a molecular-epidemiological investigation is also performed.

The age- and sex-specific incidence of AVH is calculated, using as denominator the total population of the ASLs' catchment areas. Age- and sex-specific population figures are provided by the ASLs upon enrolment in SEIEVA. The incidence rates and frequency of risk factors are

published periodically on the website of the Istituto Superiore di Sanità. Furthermore, through analytical case-control studies, the association between specific risk factors and each type of AVH is analyzed.

The diagnostic criteria used to differentiate the types of AVH are reported in Table 1.

Table 1. Diagnostic criteria used to identify acute viral hepatitis, by type

Hepatitis type	HBsAg	IgM anti-HBc	IgM anti-HAV	IgM anti-HEV	Anti-HCV and HCV RNA	Anti-Delta
A	+ - NR	+ - NR	+	+ - NR	+ - NR	+ - NR
B	+ - NR	+	- NR	- NR	+ - NR	- NR
C	+ - NR	-	-	- NR	+	- NR
E	+ - NR	- NR	-	+	+ - NR	+ - NR
Delta Coinfection	+	+	- NR	- NR	+ - NR	+
Delta Superinfection	+	-	- NR	- NR	+ - NR	+
NonA-NonE	+ - NR	-	-	-	-	- NR
Unspecified	NR	NR	NR	NR	NR	NR
Unspecified	+	- NR	- NR	- NR	+	- NR

"+" = positive, "-" = negative, "NR" = Not Reported

Cases of NonA-NonE AVH, which are clinically indistinguishable from other classical types of AVH, are characterized by having negative serological results for IgM anti-HBc, IgM anti-HAV, anti-HCV, anti-HDV and anti-HEV antibodies.

In recent years, a new condition has been identified: a particular form of viral persistence commonly termed "occult" HBV (Hepatitis B Virus) infection (OBI), that may impact, according to the emerging evidence, in several different clinical contexts (the possible transmission of the infection, the risk of reactivation, the contribution to liver disease progression and to the development of hepatocellular carcinoma) (2-4).

OBI is defined by the presence of HBV-DNA in the liver tissue (and in some cases also in the serum, but usually below 200IU/ml) of HBsAg negative individuals. Although OBI status is significantly associated with the presence of anti-HBc and/or anti-HBs antibody, more than 20% of the occult carriers are negative for all serum markers of HBV infection. Only HBV-DNA can be considered the reliable diagnostic marker of OBI.

Other cases of acute viral hepatitis NonA-NonE might be probably due to the so called minor hepatitis-related virus, such as Epstein-Barr Virus (EBV) and CytoMegaloVirus (CMV). But there are other possible known causes responsible of these cases: autoimmune diseases, Wilson disease, alcohol, mushroom intoxication, chemical agents and drugs (NSAID's, isoniazid, methotrexate, ketoconazole, antidepressant, antiretroviral and illegal compounds, such as cocaine and ecstasy).

Results of the system of surveillance

As of 31 December 2010, 138 (76.2) of the 181 ASLs in Italy participate in SEIEVA; these ASLs are distributed throughout the entire country and cover 73.1% of the national population (Figure 1).

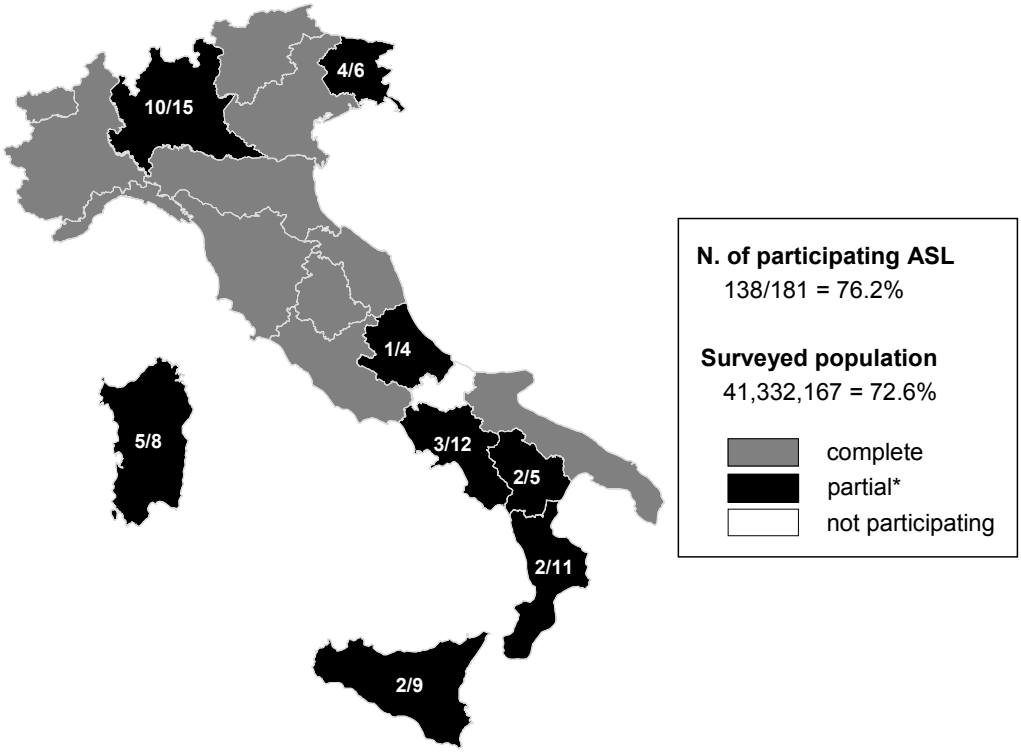


Figure 1. ASLs participating in SEIEVA as of 31 December 2010
(*the figure shows the number of participating ASLs out of the total number, by region)

Since 1987, the number of participating ASLs and thus the population coverage has gradually increased (Figure 2).

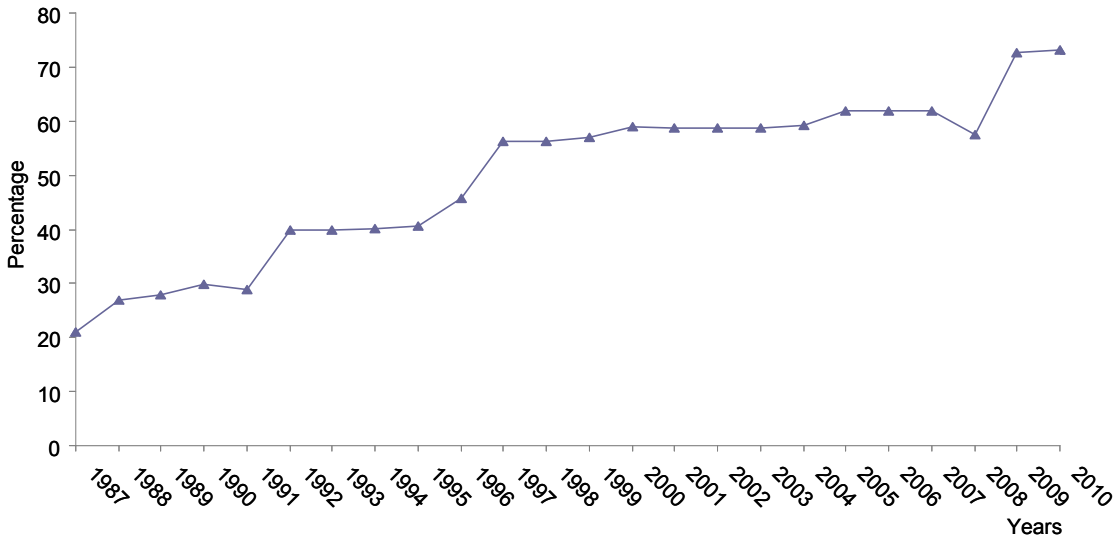


Figure 2. Percentage of Italian population covered by SEIEVA 1987-2010

General overview

In the present report, we describe epidemiological changes in AVH in the past two decades. To do so, we compared data for two periods: 1992-1994 and 2008-2010. The percentage distribution by type of AVH in 1992-1994 and 2008-2010 is shown in Figure 3. In both periods, hepatitis A was the most frequently reported type, constituting, respectively, 46% and 54% of all cases. The percentage of cases with unknown aetiology has decreased, from 12% to 4%.

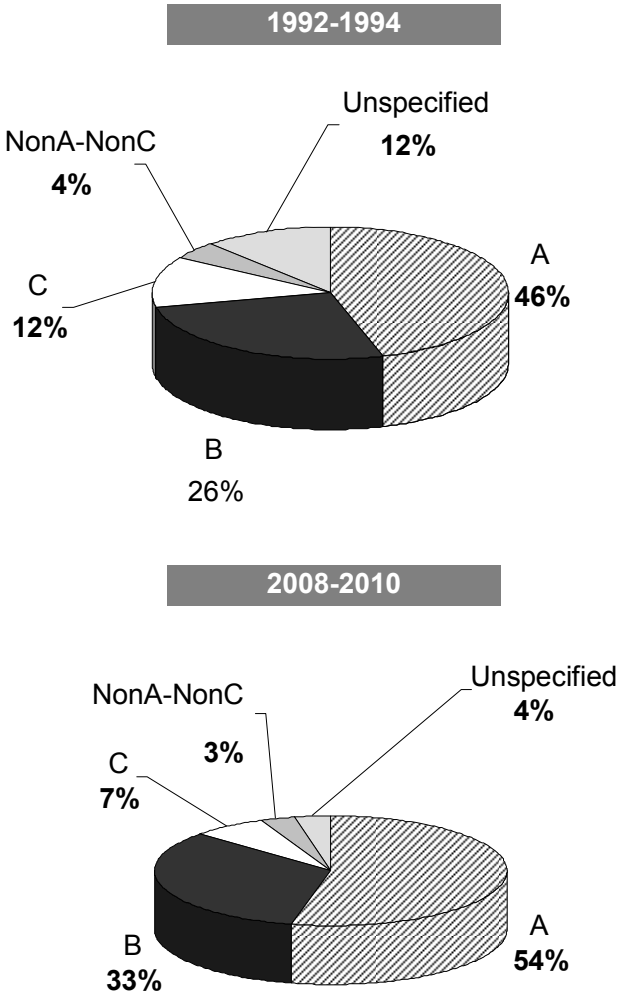
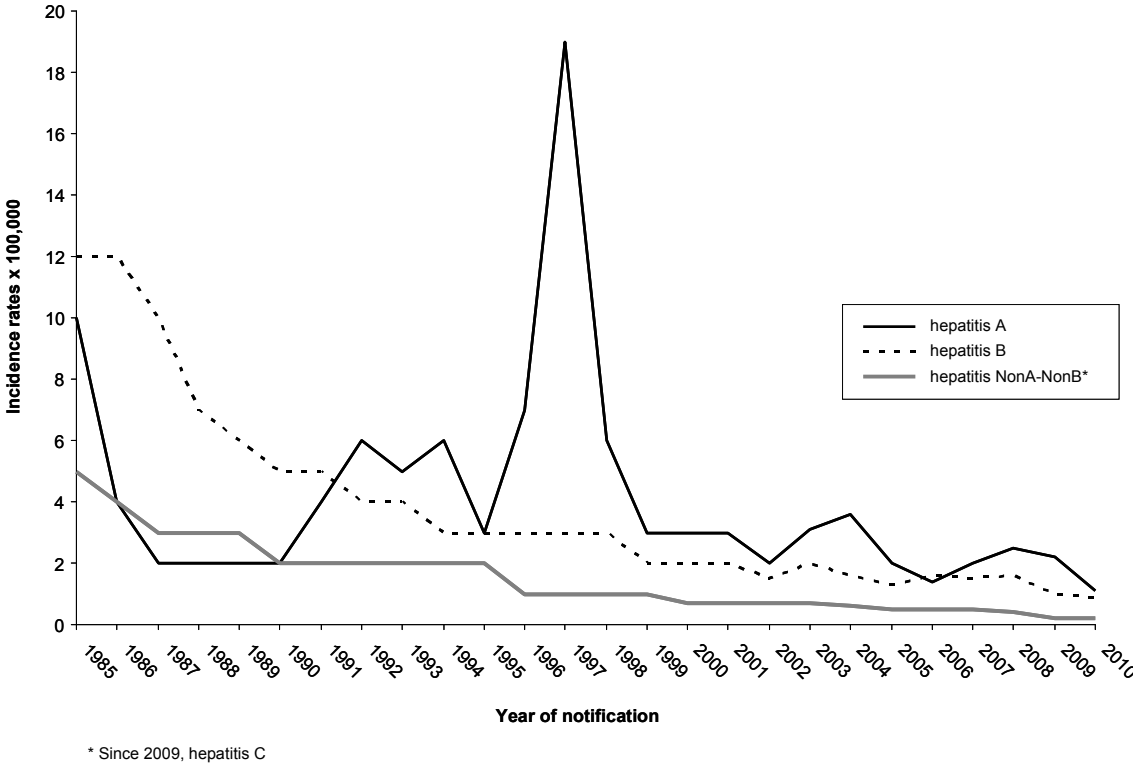


Figure 3. Distribution by hepatitis type (SEIEVA 1992-1994 and SEIEVA 2008-2010)

The incidence of AVH, by type and year, is shown in Figure 4. In the past 25 years, there has been a trend of progressive decrease in incidence for HAV, HBV, and HBC, though the decrease is more evident for HBV and HCV, as well as for Delta hepatitis (not shown in figure); these results are consistent with data provided by several seroepidemiological studies carried out in different time periods (5-9).



* Since 2009, hepatitis C

Figure 4. Incidence rates (x 100,000) of reported acute viral hepatitis, by year (SEIEVA 1985-2010)

Fatality rates

The fatality rates for AVH in 1992-1994 and 2008-2010, by type of AVH, are shown in Table 2. The fatality rate seems to have increased over time for HAV and HBV, though the increase is not statistically significant (10).

Table 2. Fatality rates per 1,000 cases of acute viral hepatitis, by type

Type of hepatitis	1992-1994			2008-2010		
	dead/cases	fatality rate	95 CI%	dead/cases	fatality rate	95 CI%
A	0/3701	0.00	0.00-1.00	5/2292	2.18	0.71-5.09
B	8/2167	3.69	1.59-7.28	12/1405	8.54	4.41-14.93
C	0/1000	0.00	0.00-3.69	2/296	6.76	0.81-24.43
NonA-NonC	0/352	0.00	0.00-10.48	2/135	14.81	1.78-53.56
Unknown	5/959	5.21	1.69-12.17	0/140	0.00	0-26.36
Total	13/8179	1.59	0.85-2.72	21/4268	4.92	3.04-7.52

The epidemiology of the different types of AVH is described in the following sections.

EPIDEMIOLOGY OF HEPATITIS A

In Italy, the epidemiology of HAV has greatly changed. According to population-based studies, the prevalence of anti-HAV antibodies has decreased in the last two decades, as a result of improved hygiene, sanitation and socio-economic conditions, so that Italy has become a country of intermediate/low endemicity (6, 11, 12).

Furthermore, among children, exposure to HAV is less common; consequently, young adults are becoming more susceptible to infection. Adults are more likely than children to have symptomatic and severe infection and complications of severe infection; complications of severe infection are also more common among persons with underlying liver damage (13, 14). Epidemic peaks occurred in 1992, 1994, and 1997 (Figure 5), in association with the consumption of raw shellfish, especially in certain regions of southern Italy (15, 16). Since 1997, there has been a trend of decrease, reaching levels similar to those in the non-epidemic period (1987-1990). The incidence in 2010 was 1.1 per 100,000 population (incidence of 1.9, 1.1, and 1.0, respectively, for the age groups 0-14, 15-24, and ≥25 years).

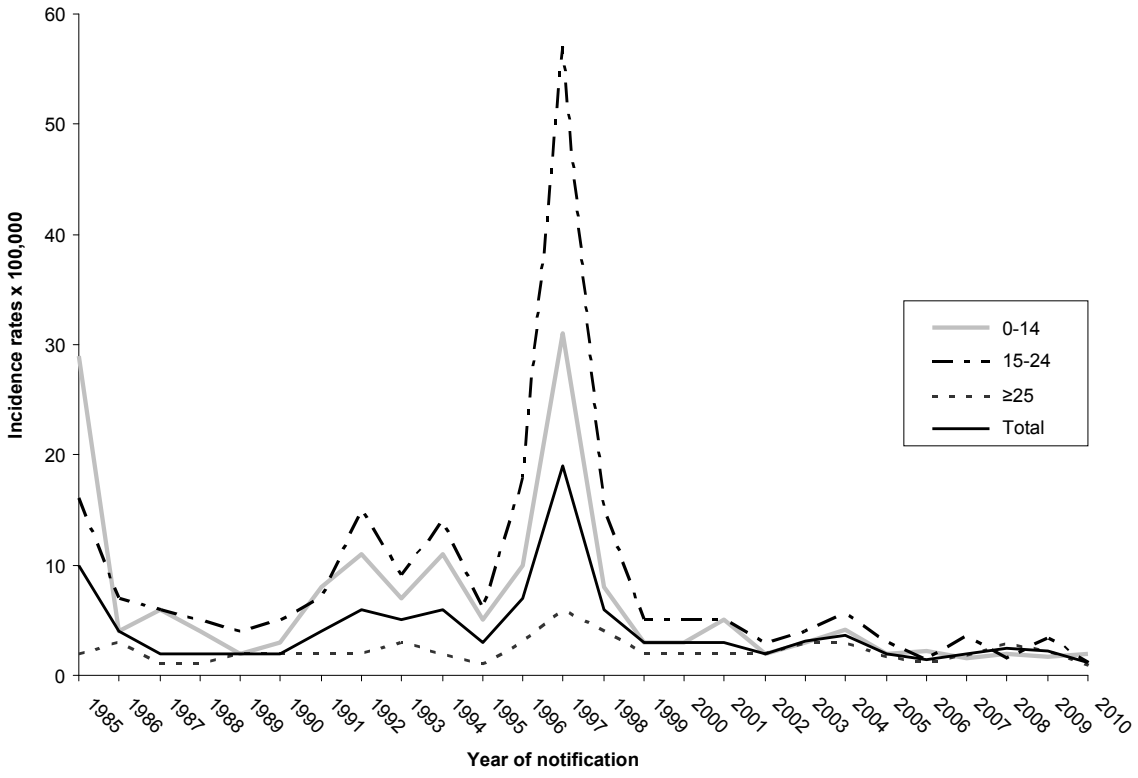


Figure 5. Incidence rates of reported acute viral hepatitis A, by year and age group (SEIEVA 1985-2010)

In the past two decades, the frequency of risk factors for HAV infection has changed due to improvements in hygiene and sanitation, a more efficient control and surveillance of shellfish retailers, and the vaccination of population groups at increased risk of infection, such as travellers to HAV-endemic countries and sewage workers (17-26).

The percent frequency of the reported risk factors for HAV infection for the periods 1992-1994 and 2008-2010 is shown in Figure 6. Shellfish consumption and travelling to areas endemic for HAV are still the most important risk factors. In 2008-2010, the percentage of cases attributable to known risk factors decreased (i.e., consumption of seafood, contact with a jaundiced person, consumption of well water). The percentage of cases attributable to travel to endemic areas has increased, as has, to an even greater extent, the percentage among men who have sex with men (MSM) (27-28). In particular, in the past few years, an excess of cases of HAV infection in MSM have been reported and outbreaks have struck the gay community in various Italian Regions. This could be explained by specific practices during sexual intercourse, such as oral-anal sex and anal-digital sex.

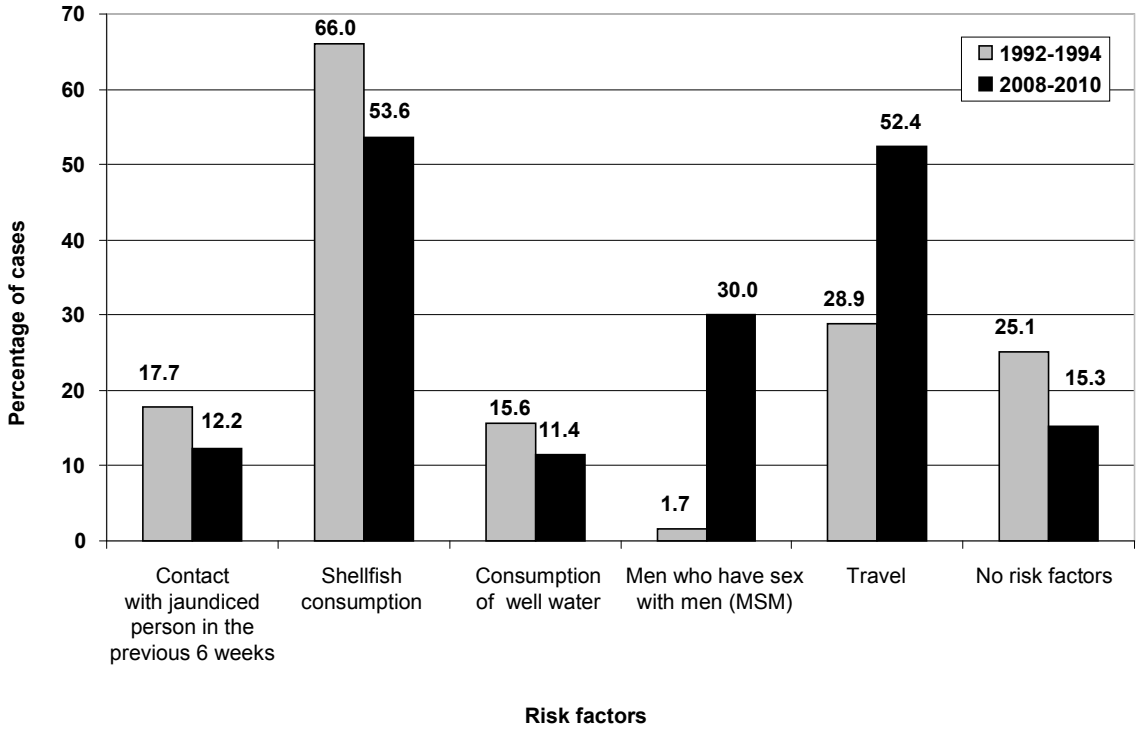


Figure 6. Percentage of risk factors reported by persons with HAV infection in Italy (SEIEVA 1992-1994 and SEIEVA 2008-2010)

The frequency (number of cases and percentage) of risk factors reported by persons with acute HAV infection in 2010 is shown in Table 3. Shellfish consumption (45%) and travel (52%) were the most frequently reported risk factors. The risk factor was unknown in 20.3% of cases.

Table 3. Risk factors reported by persons with acute hepatitis A* (SEIEVA 2010)

Risk factor	Age group (in years)							
	0-14		15-24		≥25		Total	
	n.	(%)	n.	(%)	n.	(%)	n.	(%)
Shellfish consumption	14	(14)	26	(53)	160	(55)	200	(45)
Contact with jaundiced person in the previous six weeks	18	(20)	11	(26)	28	(10)	57	(14)
Consumption of well water	29	(29.3)	10	(21.3)	24	(8.2)	63	(14.4)
Men who have sex with men (MSM)	0	(0)	4	(17.4)	29	(16.8)	33	(16.8)
Travel	58	(55)	22	(46)	154	(53)	234	(52)
No reported risk factor	29	(27.1)	7	(14.3)	57	(18.8)	93	(20.3)
Total cases of acute hepatitis A ***	106		50		303		459	

* Cases may have more than one risk factor
*** For some cases, the information on certain risk factors was not available.

EPIDEMIOLOGY OF HEPATITIS B

The epidemiology of HBV infection in Italy has changed drastically in the last two decades, as a result of the general improvement in hygienic standards and living conditions, the reduction of the mean family size, the abandonment of non-disposable syringes for administering parenteral drugs, the implementation of HBsAg screening during pregnancy and prophylaxis for newborns of positive mothers, the mandatory vaccination of infants and, until 2003, for 12-year-olds, the recommended vaccination of high-risk groups, and anti-AIDS campaigns. Consequently, Italy now has a low-intermediate level of endemicity (29-36).

The overall incidence of acute HBV infection since 1985 is shown in Figure 7. The incidence decreased from 12 per 100,000 population in 1985 to 0.9 per 100,000 population in 2010 (0.0, 0.5, and 1.2, respectively, for the age groups 0-14, 15-24, and ≥ 25 years). Although the decrease began before the implementation of universal HBV vaccination in 1991, the introduction of mandatory vaccination for all infants and for 12-year-olds further contributed to the decrease, showing a more evident impact in the age group 15-24 years. At present, the highest incidence can be found in persons aged ≥ 25 years.

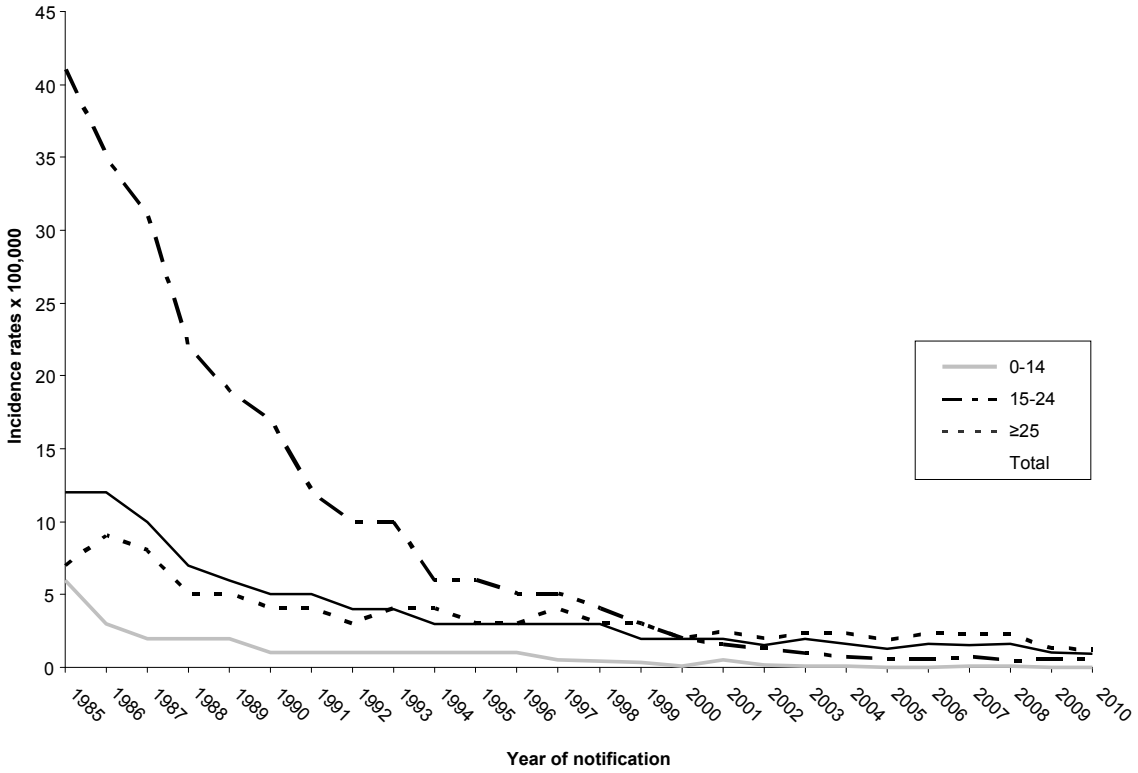


Figure 7. Incidence of reported acute viral hepatitis B infection, by year and age group (SEIEVA 1985-2010)

Before the implementation of HBsAg screening during pregnancy, prophylaxis for newborns of positive mothers and vaccination in 1991, the main risk factors for HBV infection were: vertical transmission from mother to child, living with a chronic carrier, the use of improperly sterilized medical and surgical instruments, blood transfusions, and intravenous drug use (29, 32, 33, 36-38). Since 1991, the risk factors have changed. The percent frequency of reported risk factors for HBV for the periods 1992-1994 and 2008-2010 is shown in Figure 8. In 1992-1994, the most important risk factors were intravenous drug use, cosmetic treatment with percutaneous exposure (i.e., piercing, tattooing, manicure/pedicure, and barber shop shaving, as well as acupuncture), dental therapy and promiscuous sexual activity. Compared with 1992-1994, in 2008-2010, the percentage of persons reporting intravenous drug use, cohabitation with an HBsAg-positive carrier and unsafe sexual practices (i.e., no or occasional condom use during sexual intercourse) decreased; the decrease was most evident for intravenous drug use.

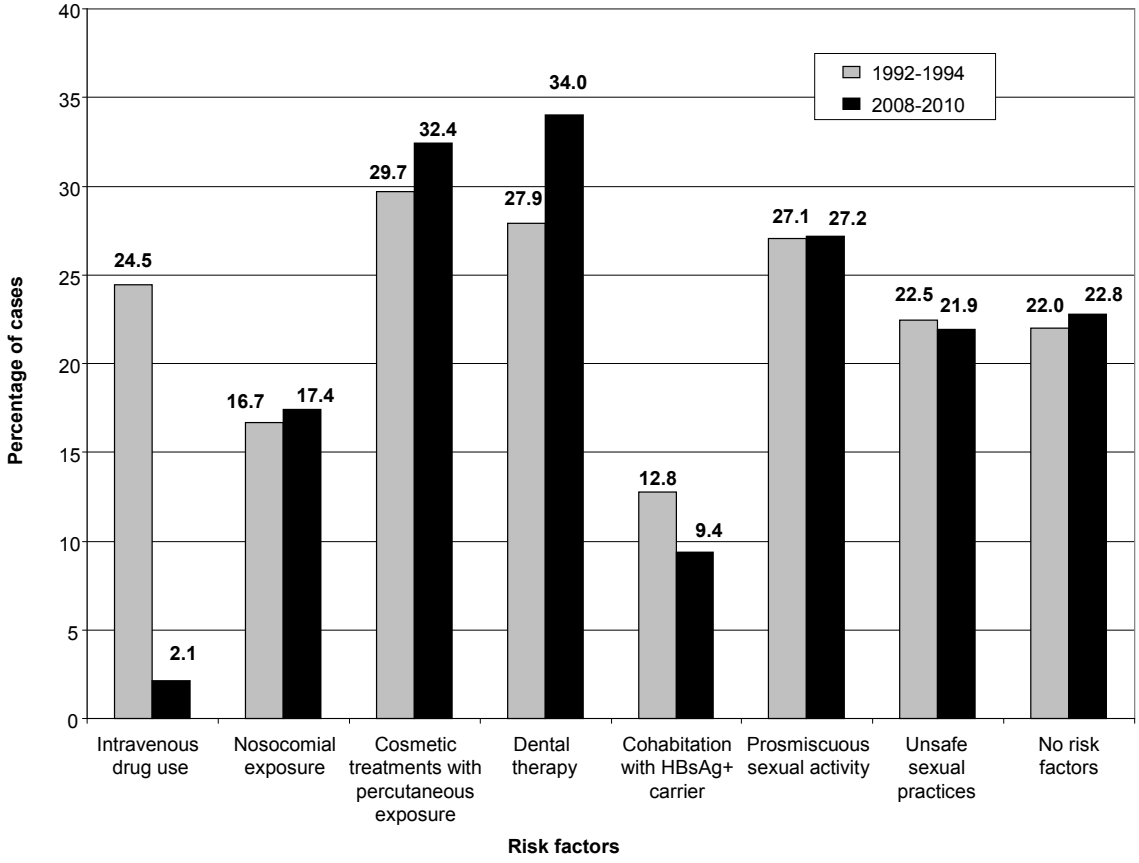


Figure 8. Risk factors reported by persons with acute HBV infection in Italy (SEIEVA 1992-1994 and SEIEVA 2008-2010)

In 2008-2010, the most important risk factors were cosmetic treatment with percutaneous exposure, dental therapy and promiscuous sexual activity; these remained the most important risk factors in 2010 (Table 4).

Table 4. Risk factors reported by persons with acute HBV infection* in Italy (SEIEVA 2010)

Risk factor	Age group (in years)							
	0-14		15-24		≥25		Total	
	n.	(%)	n.	(%)	n.	(%)	n.	(%)
Blood transfusion	0	(0)	0	(0)	8	(2)	8	(2)
Surgery	0	(0)	4	(20)	51	(14)	55	(15)
Nosocomial exposure	0	(0)	1	(5)	13	(4)	14	(4)
Cosmetic treatment with percutaneous exposure**	0	(0)	10	(50)	118	(33)	128	(34)
Dental therapy	0	(0)	7	(37)	122	(35)	129	(35)
Intravenous drug use	0	(0)	0	(0)	6	(2)	6	(2)
Living with drug user	0	(0)	0	(0)	4	(1)	4	(1)
Contact with jaundiced person in the previous six months	0	(0)	0	(0)	11	(3)	11	(3)
Promiscuous sexual activity (> 2 sexual partners in the previous six months)	0	(0)	5	(31)	114	(44)	119	(43)
Cohabitation/sexual partnership with a HBsAg+ carrier	0	(0)	2	(25)	26	(9)	28	(9)
No reported risk factor	0	(0)	4	(19.1)	79	(21.6)	83	(21.5)
Total cases of HBV infection ***	0		21		367		388	

* Cases may have more than one risk factor.
** Piercing, tattooing, manicure/pedicure, barber shop shaving and acupuncture.
*** For some cases, the information on certain risk factors was not available.

EPIDEMIOLOGY OF DELTA HEPATITIS

For infection with HDV to occur, the helper function of HBV is necessary; thus there are two types of infection: coinfection (i.e., simultaneously becoming infected with HDV and HBV) and superinfection (infection of HBsAg chronic carriers with HDV). Superinfection is associated with a more rapid progression to cirrhosis and with a higher risk of liver decompensation and hepatocellular carcinoma. A case of acute HDV infection is defined when a person is HBsAg-positive, anti-HD positive, and IgM anti-HAV negative (39, 40).

From 1987 to 2010, the incidence of HDV infection (both coinfection and superinfection) varied from 3.2 to 0.2 per million (Figure 9). In this period, 3 peaks were observed: in 1990, 1993 and, though smaller, 1997. These peaks were especially evident among 15-24 years olds (Figure 10). Intravenous drug use played an important role in the occurrence of these peaks; cohabitation with a chronic carrier of HBsAg was also important. With the exception of these three peaks, the incidence of acute HDV infection progressively decreased over time. As shown in Figure 9, this trend paralleled the trend for acute HBV infection, which began before the introduction of universal HBV vaccination. The factors that have contributed to the trend of decrease for HBV infection can probably also explain the trend for HDV infection (general improvement of hygienic standards and living conditions, decreased family size, use of disposable syringes, blood screening, anti-AIDS campaigns, vaccination of high-risk groups) (39, 40). Most of these factors probably had the greatest effect among younger persons.

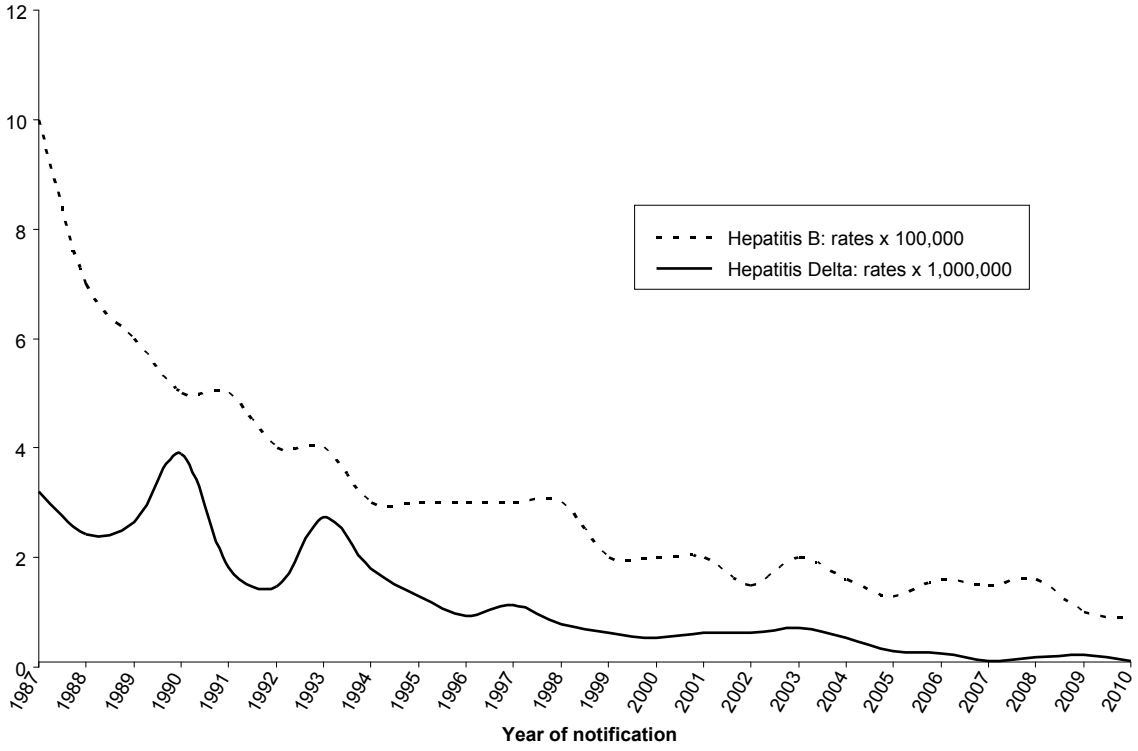


Figure 9. Incidence of acute HDV infection and incidence of acute HBV infection (SEIEVA 1987-2010)

In 2010 the incidence per 1,000,000 was 0.00, 0.00, and 0.16, respectively, for the age groups 0-14, 15-24, and ≥25 years (Figure 10). Most infections occur in persons aged ≥25 years.

Figure 10. Incidence of acute HDV infection, by year and age group (SEIEVA 1991-2010)

The percent frequency of reported risk factors for HDV infection for the periods 1992-1994 and 2008-2010 is shown in Figure 11.

In 1992-1994, the most important risk factors were intravenous drug use, promiscuous sexual activity, cosmetic treatment with percutaneous exposure, dental therapy and unsafe sexual activity. In 2008-2010, the most important risk factors were dental therapy, cosmetic treatment with percutaneous exposure and promiscuous sexual activity. With respect to 1992-1994, in 2008-2010 there was a sharp decrease in the percentage of infected individuals reporting intravenous drug use, cohabitation with an HBsAg-positive carrier, and unsafe sexual practices. There was also a decrease, though less evident, for cosmetic treatment with percutaneous exposure and promiscuous sexual activity. By contrast, there was an increase for nosocomial exposure and dental therapy; there was also an increase in the percentage of individuals with unknown risk factor.

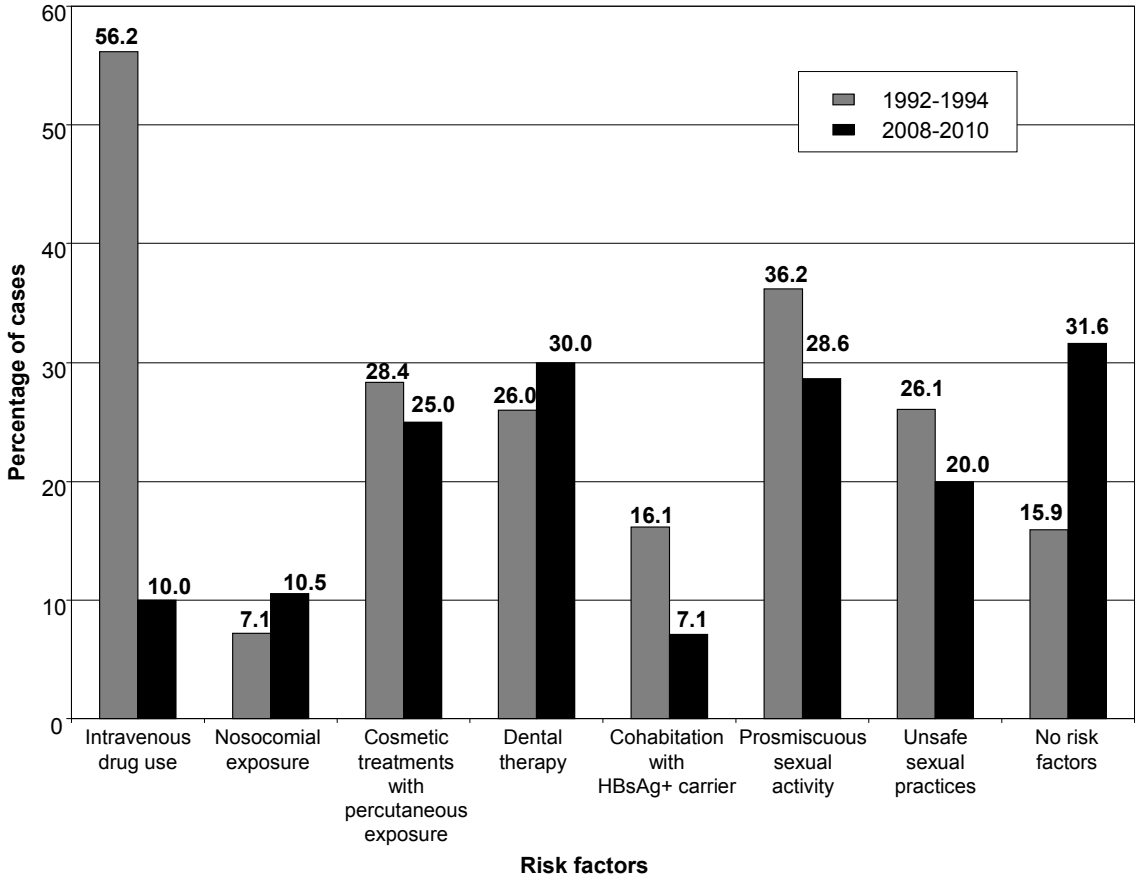


Figure 11. Risk factors reported by acute hepatitis Delta cases notified in Italy (SEIEVA 1992-1994 and SEIEVA 2008-2010)

EPIDEMIOLOGY OF HEPATITIS C

The epidemiology of infection with HCV in Italy has changed in the past two decades, with a progressive decrease in incidence and a shift in risk factors (9, 41-43). The change in risk factors can be attributed to the anti-HCV screening of blood donors (introduced in 1991) and, more recently (2001), the introduction of HCV Nucleic Acid Testing (NAT); these initiatives have led to the virtual disappearance of blood transfusion as a mode of transmission. Other contributing factors include improvements in healthcare standards and the continuous expansion of the intravenous drug use-associated HCV epidemic.

Because acute HCV infection is very often asymptomatic and the currently available assays do not distinguish between acute and chronic or resolved infection, it is difficult to calculate the incidence of HCV infection. Thus the true incidence can be underestimated. Acute cases notified to SEIEVA are diagnosed on the basis of clinical and serologic criteria (acute illness compatible with hepatitis, increase in the serum alanine aminotransferase level to 10 times the upper limit of the normal range, negativity for IgM anti-HAV and IgM anti-HBc, with positivity for anti-HCV and/or HCV-RNA). The incidence of acute HCV infection in 1985-2010, by year and age group, is shown in Figure 12 (until 2008 data refer to the infection indicated as NonA-NonB).

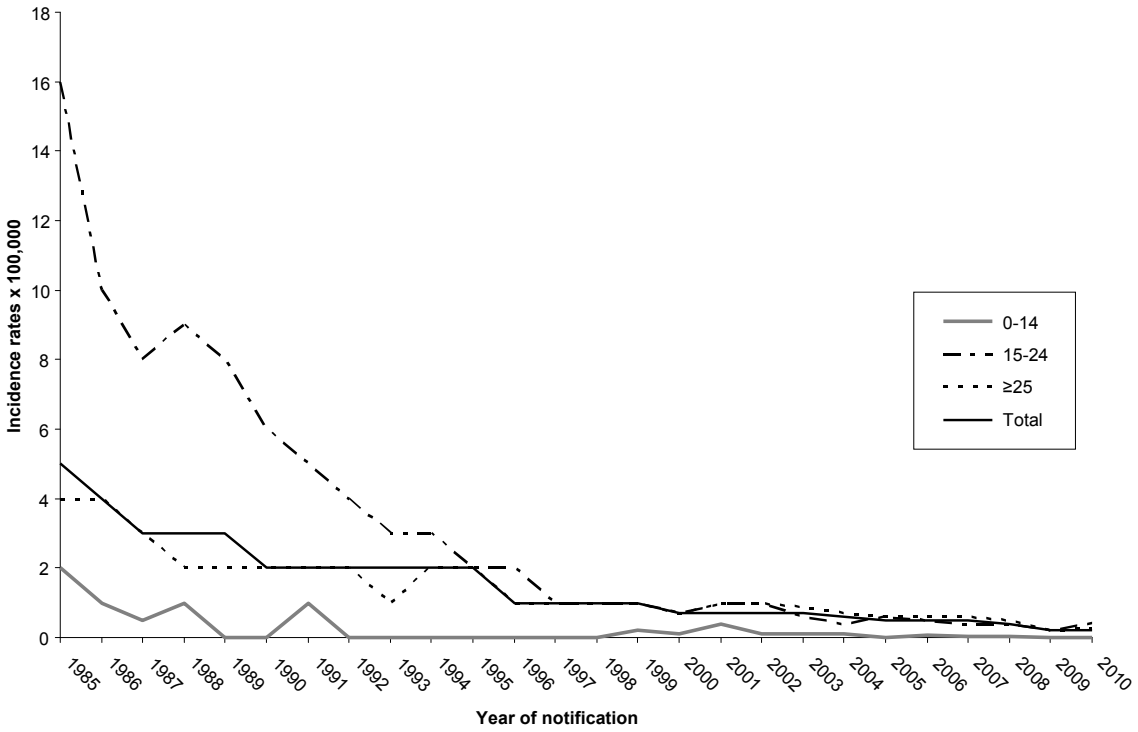


Figure 12. Incidence of reported acute HCV infection, by year and age group. (SEIEVA 1985-2010)

Overall, the incidence decreased, from 5 per 100,000 population in 1985 (2, 16, 4, respectively for age groups 0-14, 15-24, and ≥25 years) to 0.2 per 100,000 population in 2010 (0.0, 0.4, 0.2, respectively for age groups 0-14, 15-24, and ≥25 years). The greatest decrease was observed among persons aged 15-24 years, for whom the incidence was 16 per 100,000 in 1985, 2 in 1992 and 0.2 in 2010. This decrease could be due to changes in injecting behaviour among intravenous drug users and information programmes on AIDS.

The percent frequency of reported risk factors for HCV for the periods 1992-1994 and 2008-2010 is shown in Figure 13.

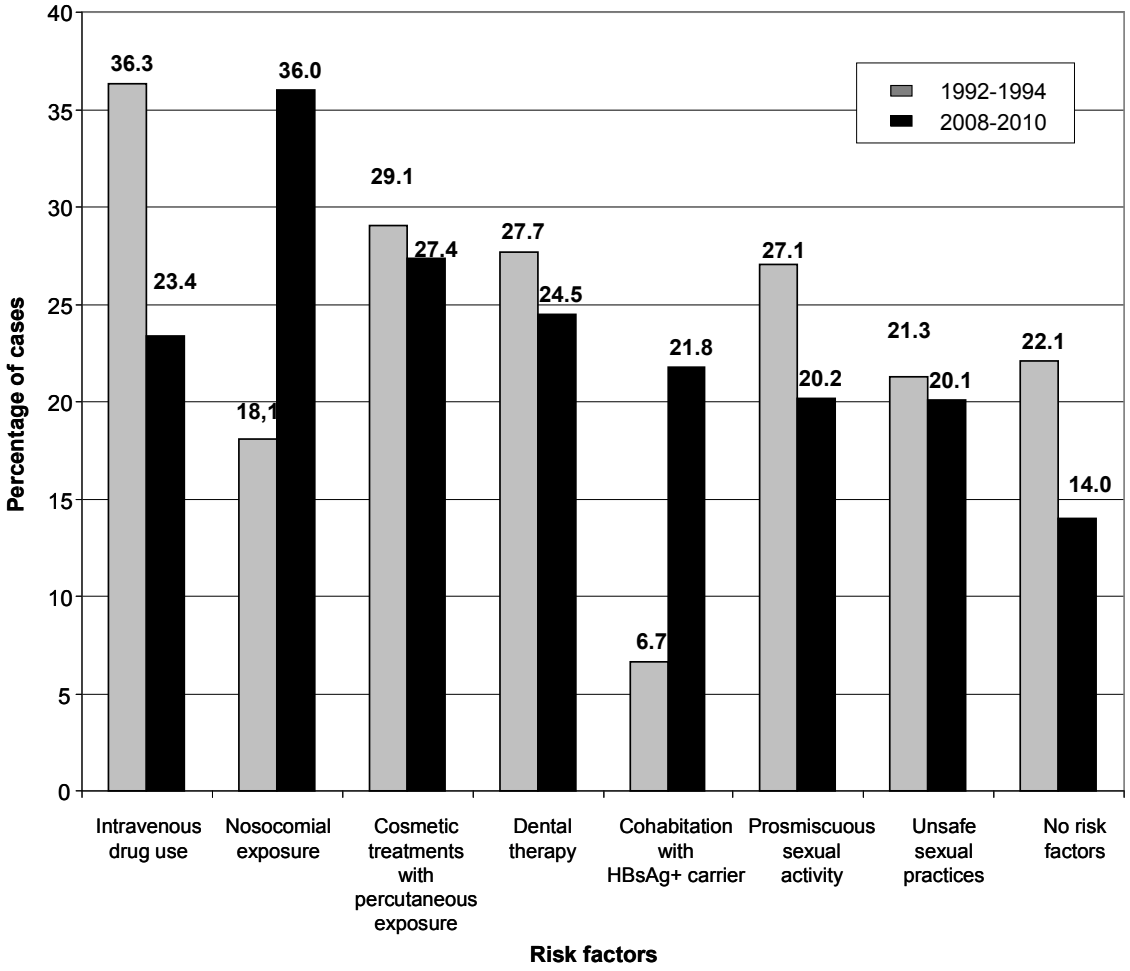


Figure 13. Risk factors reported by acute hepatitis C cases in Italy (SEIEVA 1992-1994 and SEIEVA 2008-2010)

There was a decrease in the percentages for intravenous drug use, cosmetic treatment with percutaneous exposure, dental therapy, promiscuous sexual activity, unsafe sexual practices, and unknown risk factor. By contrast, there was an increase for nosocomial exposure (which has become the most frequently reported risk factor) and cohabitation with an HCV-positive carrier. The frequency of reported risk factors for acute HCV infection in 2010, by age group, is shown in Table 5. The most frequent risk factors were: intravenous drug use, promiscuous sexual

activity, cosmetic treatment with percutaneous exposure and surgery. Among persons aged 15-24 years, the most frequent risk factors were intravenous drug use, cohabitation/sexual partnership with an HCV-positive carrier, promiscuous sexual activity and cosmetic treatment with percutaneous exposure. Among persons aged ≥ 25 years, the most frequent risk factors were surgery, cosmetic treatment with percutaneous exposure and promiscuous sexual activity (44-53).

Table 5. Risk factors reported by acute hepatitis C cases* notified in Italy (SEIEVA 2010)

Risk factor	Age group (in years)							
	0-14		15-24		≥25		Total	
	n.	(%)	n.	(%)	n.	(%)	n.	(%)
Blood transfusion	0	(0)	1	(6)	6	(8)	7	(8)
Surgery	0	(0)	1	(6)	22	(31)	23	(26)
Nosocomial exposure	0	(0)	2	(11)	5	(7)	7	(8)
Cosmetic treatment with percutaneous exposure**	0	(0)	7	(41)	19	(26)	26	(29)
Dental therapy	0	(0)	4	(24)	16	(23)	20	(23)
Intravenous drug use	0	(0)	13	(76)	13	(18)	26	(29)
Living with drug user	0	(0)	4	(24)	5	(7)	9	(10)
Contact with jaundiced person in the previous six months	0	(0)	5	(29)	3	(5)	8	(10)
Promiscuous sexual activity (> 2 sexual partners in the previous six months)	0	(0)	7	(47)	11	(27)	18	(32)
Cohabitation/sexual partnership with a HBsAg+ carrier	0	(0)	7	(41)	6	(10)	13	(17)
No reported risk factor	0	(0)	0	(0)	11	(14.7)	11	(11.6)
Total cases***	0		18		74		92	

* Cases may have more than one risk factor.
** Piercing, tattooing, manicure/pedicure, barber shop shaving and acupuncture.
*** For some cases, the information on certain risk factors was not available.

EPIDEMIOLOGY OF HEPATITIS E

Acute infection with HEV is clinically very similar to HAV infection.

Until recently, HEV infection was considered to be confined to persons who had traveled to endemic areas. However, it is now considered to be an emerging disease in industrialized countries, including Italy, where the number of indigenous cases (autochthonous infections) has increased (54-59).

Travel-related HEV infection is associated with the consumption of food or water contaminated with faeces (faecal-oral transmission).

This infection usually results in jaundice and is self-limited, though it may be particularly severe in pregnant women, especially in the third trimester.

Regarding autochthonous infection, some evidence suggests that it may be of animal origin. Recent studies in non-endemic areas have shown that the majority of autochthonous infections are caused by HEV genotype 3 (4 different genotypes have been reported), which, together with genotype 4, has a high prevalence in some animals, mainly pigs (in which infection is asymptomatic).

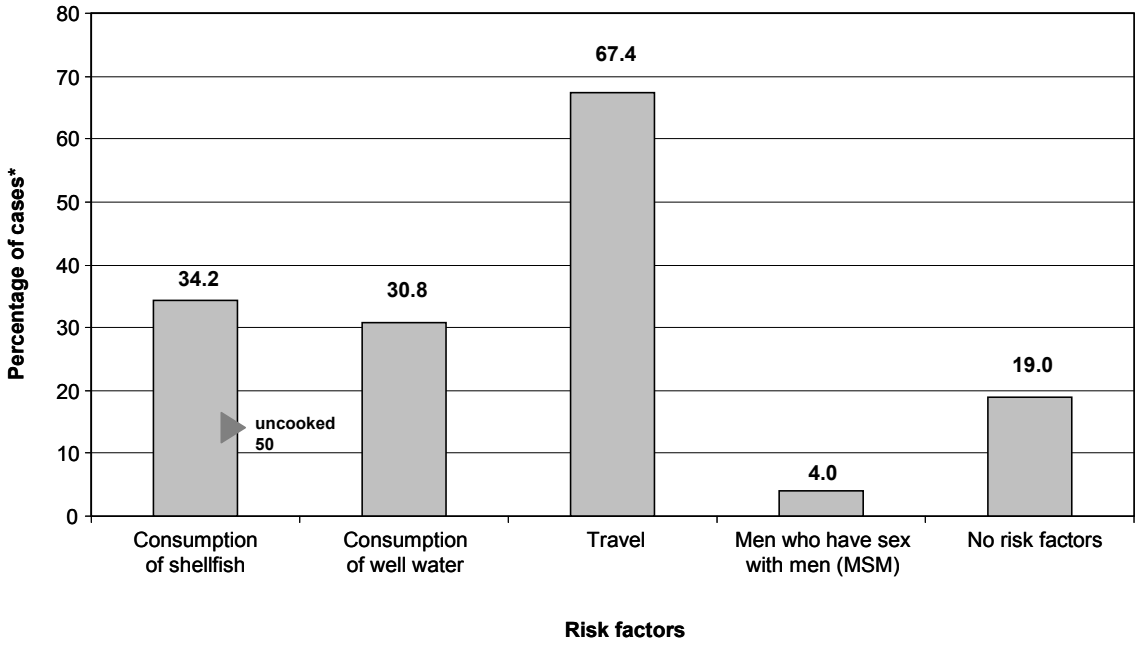
Moreover, given the close genetic homology between human and animal HEV strains, especially those infecting pigs, HEV infection is recognized as a possible zoonosis. Transmission may occur by occupational exposure (e.g., pig farmers or veterinarians), through direct contact with secretions, excretions or organs contaminated with faecal material containing the virus; it may also occur through ingestion of contaminated pork products, eaten raw or undercooked. Surface water can also be contaminated with HEV, with a significant risk for public health.

Most infections are self-limiting and asymptomatic, yet they may be persistent and more severe in immunocompromised and older (≥ 60 years) individuals.

In Italy, although several studies conducted in the 1990s reported a high prevalence of anti-HEV antibodies in humans (1-3% in north-central Italy and 3-6% in southern Italy and the Islands), the actual number of cases of acute infection reported to SEIEVA is relatively low, which can be explained by the high occurrence of sub-clinical infection. Moreover, an HEV-specific serological assay is not performed in many clinical centres.

During the period 2007-2010, 60 cases of acute HEV infection were reported to SEIEVA. Most cases occurred among persons aged 25-34 years and 35-54 years (35% and 33% of cases, respectively). Most of the infected persons (88%) were males, and 57% were from central Italy. Only 42% occurred among Italian citizens; the remaining cases were diagnosed among non-nationals from Bangladesh, India, Pakistan and Morocco.

Figure 14 shows the frequency (%) of risk factors reported by persons with acute HEV infection in the period 2008-2010. Shellfish consumption and travel in endemic areas are the most frequently reported risk factors; 19% of cases has no identified risk factor. Cases may have more than one risk factor and for some cases the information on certain risk factors is not available.



* Cases may have more than one risk factor and for some cases the information on certain risk factors is not available.

Figure 14. Risk factors reported by acute hepatitis E cases notified in Italy (SEIEVA 2007-2010)

CONCLUSIONS

In the past 25 years, there has been a trend of progressive decrease in incidence for HAV, HBV, and HBC, though the decrease is more evident for HBV and HCV, as well as for Delta hepatitis.

The prevalence of anti-HAV antibodies has decreased in the last two decades, as a result of improved hygiene, sanitation and socio-economic conditions, so that Italy has become a country of intermediate/low endemicity.

Now, among children, exposure to HAV is less common; young adults are becoming more susceptible to infection and are more likely than children to have symptomatic and severe infection and complications. The incidence of symptomatic hepatitis A is 1.1/100,000/year in interepidemic periods. Shellfish consumption and travelling to areas endemic are still the most important risk factors. Furthermore, in the past few years, an excess of cases of HAV infection in MSM have been reported and outbreaks have struck the gay community in various Italian Regions, explained by specific practices during sexual intercourse.

The epidemiology of HBV infection in Italy has changed drastically in the last two decades, as a result of the general improvement in hygienic standards and living conditions, the reduction of the mean family size, the abandonment of non-disposable syringes for administering parenteral drugs, the implementation of HBsAg screening during pregnancy and prophylaxis for newborns of positive mothers, the mandatory vaccination of infants and, until 2003, for 12-year-olds, the recommended vaccination of high-risk groups, and anti-AIDS campaigns.

Consequently, Italy now has a low-intermediate level of endemicity. The overall incidence of acute HBV infection is 0.9 per 100,000 population in 2010. At present, the highest incidence can be found in persons aged ≥ 25 years. In 2010, the most important risk factors were cosmetic treatment with percutaneous exposure, dental therapy and promiscuous sexual activity.

The factors that have contributed to the trend of decrease for HBV infection can probably also explain the trend of decrease for HDV infection.

In 2010, the incidence of HDV infection (both coinfection and superinfection) was 0.2 per million. Most infections occur in persons aged ≥25 years. In the last years, the most important risk factors were dental therapy, cosmetic treatment with percutaneous exposure and promiscuous sexual activity.

The factors that contributed to change the epidemiology of infection with HCV in Italy, in association with those responsible for decrease of HBV infection, were the anti-HCV screening of blood donors and the introduction of NAT; these factors have led to the virtual disappearance of blood transfusion as a mode of transmission, changes in injecting behaviour among IDUs and information programmes on AIDS. Currently, the incidence of symptomatic acute hepatitis C is 0.2/100,000/year. At present, the highest incidence can be found in persons aged 15-24 years.

The most important risk factors are cosmetic treatments, dental therapy, promiscuous sexual activity, intravenous drug use and surgery.

Until recently, acute infection with HEV was considered to be confined to persons who had travelled to endemic areas. However, it is now considered to be an emerging disease, with an increasing number of indigenous cases.

Travel-related HEV infection is associated with the consumption of food or water contaminated with faeces (faecal-oral transmission). Regarding autochthonous infection, some evidence suggests that it may be of animal origin.

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